

UNITED STATES DISTRICT COURT  
EASTERN DISTRICT OF NEW YORK

COLLAGENEX PHARMACEUTICALS, INC. and  
THE RESEARCH FOUNDATION OF  
STATE UNIVERSITY OF NEW YORK,

Plaintiffs,

v.

IVAX CORPORATION,  
IVAX PHARMACEUTICALS, INC.,  
and COREPHARMA, LLC

Defendants.

CV 04 4253  
TOWNES, J.  
POHOORECKY, M.J. COMPLAINT AND  
JURY DEMAND

FILED  
IN CLERK'S OFFICE  
U.S. DISTRICT COURT E.D.N.Y.

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BROOKLYN OFFICE

Plaintiffs, CollaGenex Pharmaceuticals, Inc. ("CollaGenex") and the Research Foundation of State University of New York ("The Research Foundation"), for their Complaint against Defendants, IVAX Corporation and IVAX Pharmaceuticals, Inc. (collectively "IVAX"), and CorePharma, LLC ("CorePharma"), allege as follows:

THE PARTIES

1. CollaGenex is a publicly traded corporation organized under the laws of the state of Delaware and having a principal place of business at 41 University Drive, Newtown, Pennsylvania 18940.

2. The Research Foundation is a private, non-profit educational corporation whose primary responsibility is the administration of externally funded contracts and grants for and on behalf of the State University of New York. The Research Foundation is organized

under the laws of the State of New York and has a principal place of business at 35 State Street, Albany, New York 12201-0009.

3. On information and belief, IVAX Corporation is a corporation organized under the laws of the state of Florida, and having a principal place of business at 4400 Biscayne Blvd., Miami, Florida 33137.

4. On information and belief, IVAX Pharmaceuticals, Inc. is a corporation organized under the laws of the state of Florida, and having a principal place of business at 4400 Biscayne Blvd., Miami, Florida 33137.

5. On information and belief, IVAX Pharmaceuticals, Inc. is a wholly-owned subsidiary of IVAX Corporation.

6. On information and belief, CorePharma is a limited liability company organized under the laws of the state of New Jersey, and having a principal place of business at 215 Wood Ave., Middlesex, NJ 08846.

#### JURISDICTION AND VENUE

7. This Court has subject matter jurisdiction of this action pursuant to 28 U.S.C. §1331 and 1338(a).

8. This Court is empowered to provide declaratory judgment as a remedy in this action pursuant to 28 U.S.C. §2201 and §2202.

9. On information and belief, IVAX and CorePharma have contacts with New York as follows:

- i) Does business in New York generally;
- ii) Employs and/or engages agents and/or representatives in New York to perform services on its behalf;
- iii) Has substantial sales of pharmaceutical products in New York; and
- iv) Advertises in trade journals or other written and/or printed materials in hard copy and/or electronically directed to residents and companies in the state of New York.

10. Thus, on information and belief, IVAX and CorePharma, either separately or in cooperation with other companies and/or their agents, each has a presence in the state of New York amounting to a continuous course of conduct in New York and/or has sufficient contacts with the state of New York such that of assertion of *in personam* jurisdiction over IVAX and CorePharma comports with the requirements of due process and notions of fairness.

11. Venue is proper in this district pursuant to 28 U.S.C. §1391(b), §1391(c) and §1400(b).

**COLLAGENEX PHARMACEUTICALS, INC.**

12. CollaGenex is a specialty pharmaceutical company which provides innovative medical therapies for targeted disease classes. CollaGenex currently services the dental and dermatology markets. CollaGenex's flagship product is Periostat®, an oral enzyme suppressing-agent and bone protein-enhancing agent. Periostat® provides the first and only systemic pharmaceutical treatment for adult periodontitis, which works by: i) inhibiting the enzymes which destroy periodontal support tissue(s); and ii) enhancing bone protein synthesis.

13. CollaGenex is a publicly traded company which is primarily based on a core technology originating from research conducted at the laboratories of the State University of New York at Stony Brook by Dr. Lorne M. Golub. Dr. Golub, et al. discovered certain unique properties of tetracycline compounds, such properties being the subject of a series of U.S. patents (assigned to The Research Foundation) which are exclusively licensed to CollaGenex.

14. Over the years, CollaGenex has invested over 70 million dollars in the development of Periostat® as a Food and Drug Administration (FDA)-approved, American Dental Association (ADA)-accepted, prescription drug for use in the treatment of adult periodontitis, and has actively engaged in marketing and sales of Periostat® throughout the world.

15. Periostat® is CollaGenex's primary product, and its (i) commercial reputation, (ii) maintenance of primary income stream, and (iii) value of the company, reside in sustaining the premier market position of Periostat®.

**PERIOSTAT®**

16. One way Periostat® works is by reducing the activity of the enzymes which destroy tooth and gum tissue.

17. Periostat® also works by enhancing bone protein synthesis, and has been shown to reduce pocket depth and promote attachment level gain in patients suffering from adult periodontitis.

18. Periostat® is available only by prescription from a dentist or periodontist or physician.

19. Periostat® is a tablet containing 20mg of doxycycline hydclate. This tablet is taken twice a day by the patient. Extensive research conducted by Dr. Golub and CollaGenex established that this dose and dosage regimen delivers a sub-antimicrobial dosage of the active ingredient doxycycline hydclate, which unexpectedly is both safe and effective for long term administration to patients. Periostat® differs fundamentally from other formulations of tetracycline and its derivatives in that it is a tetracycline compound and dosage form proven safe for long term administration. As demonstrated in CollaGenex's New Drug Application (NDA), treatment with Periostat® does not affect the number of resident microflora of the body and does not contribute to the development of antimicrobial resistance.

20. On the basis of clinical trials set forth in the NDA, CollaGenex obtained FDA approval of Periostat® for the treatment of adult periodontitis.

**PATENTS COVERING PERIOSTAT®**

21. The use of the Periostat® product for the treatment of adult periodontitis is covered by U.S. Patent No. 4,666,897 (Exhibit A) and Re-Issue Patent RE 34,656 (Exhibit B) referred to herein collectively as the "patents in suit." The '897 patent expired on May 19, 2004; while the RE 34,656 patent does not expire until May 15, 2007. Both patents in suit are printed on the package insert for Periostat® whereby notice under 35 U.S.C. § 287 is provided.

22. Both of these patents have been issued to Dr. Golub, et al. and have been assigned to The Research Foundation.

23. These patents and other patents relating to Dr. Golub's technology are exclusively licensed to CollaGenex. Under the license from The Research Foundation, CollaGenex has the authority to enforce the rights provided by the patents in suit.

**PRIOR ENFORCEMENT OF THE PATENTS IN SUIT**

24. The patents in suit have been successfully enforced in three separate actions. All three of the actions concluded with a consent decree and injunction, ordered by the court.

25. The first action was against Thrifty Pharmacy III, Inc. ("Thrifty"). In the consent decree executed by Thrifty, Thrifty agrees and the court ordered that Thrifty be enjoined from using, compounding, making, manufacturing, selling, offering to sell, or

advertising for sale any substitute or replacement for Periostat® not approved by the FDA. A copy of the consent decree entered into by Thrifty is attached as Exhibit C.

26. In the other two actions, CollaGenex enforced its patents against generic drug manufacturers and their related companies for submitting ANDAs seeking approval to market a generic form of Periostat®. The first action involving a generic drug manufacturer was enforced against West-ward Pharmaceutical Corp., Nabil Rizk, Hal Eckard, North Point Pharmaceutical Research #1, L.L.C., Hikma Investment, and NPH, L.L.P. (collectively “West-ward”). In the consent judgment, West-ward admitted that both of the patents in suit are valid and infringed by submitting and seeking approval of an abbreviated new drug application (ANDA) under §505(j) of the Federal Food, Drug, and Cosmetic Act for a generic version of CollaGenex’s Periostat®. West-ward also confessed that the unauthorized (i.e. unlicensed) marketing, sale and offer for sale of a generic form of Periostat® would make each of the defendants liable as an inducer of infringement under 35 U.S.C. §271(b) and/or as a contributory infringer under 35 U.S.C. §271(c). A copy of the consent decree entered into by West-ward is attached as Exhibit D.

27. In the other action involving a generic drug manufacturer, CollaGenex enforced its patents against Mutual Pharmaceutical Company, Inc. (“Mutual”) and United Research Laboratories, Inc. (collectively “Mutual/URL”). In the consent decree concluding the action against Mutual/URL, Mutual/URL admit that the patents in suit are valid, and that the commercial manufacture, use, sale importation and offer for sale of a generic version of CollaGenex’s Periostat® for which Mutual submitted its ANDA would infringe both of the

patents in suit. A copy of the consent decree entered into by Mutual/URL is attached as Exhibit E.

**INFRINGEMENT UNDER 35 U.S.C. § 271(c)(2)(A)**

28. The patents in suit cover the use of Periostat® to treat patients with adult periodontitis.

29. Specifically, the two patents cover the treatment of patients by use of Periostat® since it reduces a pathological excess of collagenolytic enzyme activity in patients in need thercof and since it enhances bone protein synthesis in patients with bone deficiency disorders, such as periodontitis.

30. On information and belief, IVAX and CorePharma each provide generic drugs to the marketplace.

31. IVAX and CorePharma have each submitted an Abbreviated New Drug Application (“ANDA”) under § 505(j) of the Food, Drug and Cosmetic Act (“FDCA”) for a 20 mg dosage of doxycycline for treating periodontitis, which is near approval by the FDA. See Declaration of IVAX’s President, Rafick Henein, at ¶’s 5 and 6 and Exhibit B to that Declaration, attached hereto as Exhibit F. See Declaration of CorePharma’s Vice President, Scientific Affairs, Mukteeshwar Gande, at ¶’s 3-6, and Exhibit A attached to that Declaration, attached hereto as Exhibit G.

32. In accordance with the FDA requirements, the package insert for the IVAX and CorePharma products must be substantially identical to the package insert in

CollaGenex's Periostat® packaging. See, 21 C.F.R. §314.94. Accordingly, the package insert for the generic Periostat® to be sold by IVAX and CorePharma will instruct the periodontist, pharmacist, dentist and patient suffering from adult periodontitis to administer their generic version of Periostat® twice a day (b.i.d.) for a prolonged period of time, as described in CollaGenex's package insert. A copy of CollaGenex's package insert for Periostat® is attached as Exhibit H.

33. Therefore, IVAX and CorePharma have each committed an act of infringement and continue to infringe under 35 U.S.C. § 271(e)(2)(A) which states as follows:

“§ 271...

...(e)...

(2) It shall be an act of infringement to submit

(A) an application under section 505(j) of the Federal Food, Drug, and Cosmetic Act or described in section 505(b)(2) of such Act for a drug claimed in a patent or the use of which is claimed in a patent,

...

if the purpose of such submission is to obtain approval under such Act to engage in the commercial manufacture, use, or sale of a drug or veterinary biological product claimed in a patent or the use of which is claimed in a patent before the expiration of such patent.”

34. On information and belief, IVAX and CorePharma each willfully and wantonly submitted its application under § 505(j) with full knowledge of the patents in suit and in complete disregard of CollaGenex's and The Research Foundation's legitimate patent rights.

35. Thus, IVAX and CorePharma have each engaged in infringing activity under 35 U.S.C. §271(c)(2)(A), with full knowledge of the patents-in-suit.

36. In accordance with 35 U.S.C. § 271(c)(4)(A) CollaGenex and The Research Foundation are entitled to an order from the Court requiring that the date of approval of the applications under §505(j) by IVAX and CorePharma be no earlier than the date of the last to expire of patents in suit, *i.e.*, May 15, 2007.

37. Further, in accordance with 35 U.S.C. § 271(e)(4)(B), CollaGenex and The Research Foundation are entitled to injunctive relief against IVAX and CorePharma to prevent the commercial manufacture, use, offer to sell, and sale within the United States and importation into the United States of 20 mg dosages of doxycycline for the treatment of periodontitis.

#### **INFRINGEMENT UNDER 35 U.S.C. § 271(b)**

38. Plaintiffs incorporate by reference the allegations of paragraphs 1 through 37.

39. Upon information and belief, IVAX and CorePharma have each indicated that it intends to market and sell a generic version of Periostat® (20 mg dosages of doxycycline hyclate for the treatment of periodontitis) upon approval of its application under § 505(j). See ¶ 7 of Exhibit F (IVAX) and ¶ 3-6 of Exhibit G (CorePharma).

40. Once approved by the FDA, IVAX and CorePharma will be providing detailed instructions and information for use of its generic version of Periostat® by including a package insert with their generic product. The package insert will describe a method of

treatment of periodontitis which includes the treatments covered by the claims of the patents in suit, and will induce the patients, dentists and periodontists to infringe the RE 34,656 patent.

41. Upon information and belief, IVAX and CorePharma will be conducting marketing, advertising and otherwise promoting its 20 mg dosages of doxycycline for the treatment of periodontitis upon approval of its ANDA by the FDA. In so doing, IVAX and CorePharma will be trading on and/or invoking the marketing, good will and product claims of CollaGenex, established through CollaGenex's own marketing, sales and training of the profession (e.g., periodontists).

42. The offer for sale, sale and/or marketing of a 20 mg dosage of doxycycline for the treatment of periodontitis by IVAX and CorePharma, in accordance with CollaGenex's marketing and labeling of Periostat®, induces others to infringe CollaGenex's and The Research Foundation's patent claims and renders IVAX and CorePharma liable as an infringer for inducement under 35 U.S.C. §271(b).

43. The aforementioned actions of IVAX and CorePharma, including submitting the application under § 505(j) and marketing and offering for sale 20 mg dosages of doxycycline were taken willfully and wantonly in complete disregard of CollaGenex's and The Research Foundation's legitimate patent rights.

44. Consequently, CollaGenex and The Research Foundation are entitled to injunctive relief under 35 U.S.C. §283 from the infringing activity of IVAX and CorePharma.

45. Furthermore, CollaGenex and The Research Foundation are entitled to damages under 35 U.S.C. §284 resulting from the infringing activities of IVAX and CorePharma, including treble damages and attorneys fees under 35 U.S.C. §285 as the Court may find.

**INJURY**

46. IVAX and CorePharma, upon FDA approval, are each poised to introduce its product into the commercial marketplace which, in use, will infringe the Plaintiffs' patents and which will have irrevocable impact on the reputation, product and sales, and the very viability of CollaGenex as a company.

47. Unless enjoined, IVAX and CorePharma intend to and will continue a course of conduct which will infringe the patents in suit. As a direct and proximate result of the acts of IVAX and CorePharma, CollaGenex will suffer irreparable harm and sustain untold loss of revenue, reputation, and stock value. CollaGenex has no adequate remedy at law to redress such injuries that IVAX and CorePharma intend to cause and will cause by their conduct.

48. CollaGenex and The Research Foundation are entitled to an injunction restraining IVAX and CorePharma, their officers, agents, employees, and all persons acting in concert with IVAX and CorePharma, from engaging in any further acts related to the infringement of the patents in suit; and to damages and attorney fees as set forth in the statute.

**PRAYER FOR RELIEF**

**WHEREFORE**, CollaGenex and The Research Foundation pray for an order:

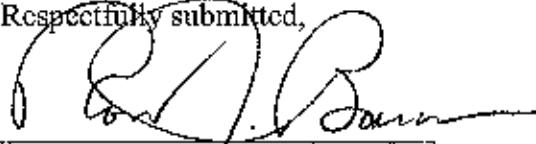
- a. Requiring that the effective date of any approval by the FDA of 20 mg doxycycline dose applied for by IVAX and CorePharma be not earlier than the date of expiration of the last to expire of the patents in suit; *i.e.*, not earlier than May 15, 2007;
- b. Imposing injunctive relief against IVAX and CorePharma to prevent the commercial manufacture, use, offer to sell, and sale within the United States and importation into the United States of a 20 mg doxycycline generic version of Periostat®;
- c. Adjudging that IVAX and CorePharma have infringed U.S. Patent No. 4,666,897 and RE 34,656 under 35 U.S.C. § 271(e)(2) by each submitting an application under Section 505(j) of the Federal Food, Drug and Cosmetic Act for the purpose of obtaining approval under such Act to engage in the commercial manufacture, use, or sale of a drug, the use of which is claimed in a patent before the expiration of the patent;
- d. Declaring that IVAX and CorePharma will infringe U.S. Patent RE 34,656 under 35 U.S.C. §271(b), by introducing, upon FDA approval, the 20 mg doxycycline drug to the marketplace for the treatment of periodontitis;
- e. Declaring that any of the acts of sales, offer for sale, and importation into the United States of a 20 mg doxycycline generic version of Periostat® will infringe U.S. Patent RE 34,656;

- f. Enjoining IVAX and CorePharma, its officers, agents, servants, employees and attorneys and all those persons acting in concert or participation with IVAX and CorePharma from infringing the patents in suit;
- g. Enjoining IVAX and CorePharma, its officers, agents, servants, employees and attorneys and all those persons acting in concert or participation with IVAX and CorePharma from marketing or offering for sale generic Periostat® in the manner prescribed on the label and package insert;
- h. Awarding to CollaGenex and The Research Foundation any damages incurred by acts undertaken by IVAX and CorePharma for infringement of the patents-in-suit, including damages for lost orders and sales, corrective advertising and attorneys fees;
- i. Requiring IVAX and CorePharma to take all actions necessary to prevent introduction of infringing product into commerce in the United States;
- j. Awarding to CollaGenex and The Research Foundation as against IVAX and CorePharma aggravated damages up to three times the amount assessed and the cost of the suit, including attorneys fees; and

k. Such other further relief as the Court deems just.

This the 1<sup>st</sup> day of October, 2004.

Respectfully submitted,

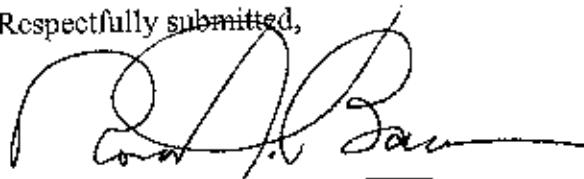


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JURY DEMAND

CollaGenex and The Research Foundation hereby demand a trial by jury on all issues triable to jury.

Respectfully submitted,



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